The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 31

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte LINDA G. CIMA, EDWARD W. MERRILL,
and PHILIP R. KUHL

Appeal No. 1999-0965
Application 08/398,555

HEARD: MAY 22, 2001

Before WINTERS, ROBINSON, and ADAMS Administrative Patent Judges.

WINTERS, Administrative Patent Judge.

DECISION ON APPEAL

This appeal was taken from the examiner's decision rejecting claims 1 through 32, which are all the claims pending in the application.

REPRESENTATIVE CLAIMS

Claims 1, 13, 31, and 32, which are illustrative of the subject matter on appeal, read as follows:

1. A composition for stimulating the growth of eukaryotic cells comprising
a biocompatible solid substrate,
biocompatible synthetic polymeric tethers, and
growth effector molecules,
wherein one end of each tether is covalently linked to the substrate and each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be internalized by cells attached to the substrate, and the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules.

13. A method for growing eukaryotic cells comprising bringing into contact the cells and a composition comprising
a bicompatible solid substrate,
bicompatible polymeric tethers, and
growth effector molecules,
wherein one end of each tether is covalently linked to the substrate and each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be internalized by cells attached to the substrate, and the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules; and
maintaining the contacting cells and composition under conditions and for a time sufficient to cause the cells to grow.

31. A cell culture comprising
a biocompatible solid substrate,
biocompatible polymeric tethers,
growth effector molecules, and
growing cells,
wherein one end of each tether is covalently linked to the substrate and each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be internalized by cells attached to the substrate, and the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules, and wherein the growing cells are bound to the growth effector molecules.

32. A method of testing a compound for an effect on tissue comprising
bringing into contact the compound to be tested and a composition comprising
a biocompatible solid substrate,
biocompatible polymeric tethers,
growth effector molecules, and
growing cells,

wherein one end of each tether is covalently linked to the substrate and each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be internalized by cells attached to the substrate, and the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules, and wherein the growing cells are bound to the growth effector molecules;

incubating the compound and the composition under conditions promoting cell growth, and

observing the cells for any effect not observed in cells not brought into contact with the composition [sic, compound].

THE REFERENCES

The prior art references relied on by the examiner are:

Naughton et al. (Naughton)	5,032,508	Jul. 16, 1991
Merrill (Merrill '264)	5,171,264	Dec. 15, 1992
Herweck et al.(Herweck)	5,370,681	Dec. 6, 1994
Clapper et al. (Clapper)	5,512,474	Apr. 30, 1996
Mikos	5,522,895	Jun. 4, 1996
Sakai Enex (EP '733)	EP 531,733	Mar. 17, 1993
Bio-Metric Systems (PCT '616)	WO 89/05616	Jun. 29, 1989

Edward W. Merrill "Poly(ethylene oxide) star molecules: Synthesis, characterization, and applications in medicine and biology," Journal Biomaterial Science Polymer, Vol. 5, No.1/2, pages 1-11, (1993)

Tomomura et al. (Tomomura), "The Control of DNA Synthesis in Primary Cultures of Hepatocytes From Adult and Young Rats: Interactions of Extracellular Matrix Components, Epidermal Growth Factor, and the Cell Cycle," Journal of Cellular Physiology, Vol. 30, pages 221-227 (1987)

THE REJECTIONS

The appealed claims stand rejected as follows: (1) Claims 1 through 32 under 35 U.S.C. § 112, second paragraph, as indefinite for not particularly pointing out and distinctly claiming the subject matter which applicants regard as their invention; (2) claim 8 under 35 U.S.C. § 112, fourth paragraph, as constituting an improper dependent claim; (3) claims 1 through 9, 13, 18 through 25, and 31 under 35 U.S.C. § 102(b) as described by Clapper; (4) claims 10 through 12 and 26 through 28 under 35 U.S.C. § 103(a) as unpatentable over Clapper; (5) claims 1 through 9, 13 through 16, 18 through 25, and 31 under 35 U.S.C. § 103(a) as unpatentable over Herweck in view of Merrill '264; (6) claims 10 through 12 and 26 through 28 under 35 U.S.C. § 103(a) as unpatentable over Herweck in view of Merrill '264 and Merrill (J. Bio-Mater. Sci. Polymer); (7) claim 17 under 35 U.S.C. § 103(a) as unpatentable over Herweck in view of Merrill '264 and Mikos; (8) claims 29 and 32 under 35 U.S.C. § 103(a) as unpatentable over Herweck in view of Merrill '264 and Naughton; (9) claims 29 and 30 under 35 U.S.C. § 103(a) as unpatentable over Herweck in view of Merrill '264 and Tomomura; (10) claims 1 through 7, 9, 10, 13, 18 through 21, 23, 25, 26, 29, 30, and 31 under 35 U.S.C. § 102(b) as described by EP '733; (11) claims 10 through 12 and 26 through 28 under 35 U.S.C. § 103(a) as unpatentable over EP '733; (12) claims 1 through 10, 12 through 26, 28, and 31 under 35 U.S.C. § 102(b) as described by PCT '616; and (13) claims 11 and 27 under 35 U.S.C. § 103(a) as unpatentable over PCT '616.

DELIBERATIONS

Our deliberations in this matter have included evaluation and review of the following materials: (1) the instant specification, including Figures 1 and 2, and all the claims on appeal; (2) applicants' main Brief received November 28, 1997, and the Reply Brief received March 16, 1998; (3) the Examiner's Answer mailed January 12, 1998 (Paper No. 25); (4) the above-cited prior art references relied on by the examiner; and (5) U.S. Patent No. 5,906,828 issued May 25, 1999, to Cima et al.

On consideration of the record, including the above-listed materials, we affirm the examiner's decision rejecting claims 1 through 13 and 18 through 31. We reverse the examiner's decision rejecting claim 32. We vacate the decision rejecting claims 14 through 17 on prior art grounds and remand this application for further consideration of those claims. Our reasons supporting this decision are set forth below.

35 U.S.C. § 112, SECOND PARAGRAPH

All of the appealed claims recite that "growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules." According to the examiner, the claims are indefinite in view of that recitation. The examiner argues that "to enhance the rate of target cell growth" is indefinite because "enhance" is a relative term (Examiner's Answer, page 4). We disagree. For the reasons succinctly stated in applicants' Appeal

Brief, page 13, first full paragraph, we conclude that any person skilled in the art can reasonably ascertain the scope of the claimed compositions and methods.

The rejection of claims 1 through 32 under 35 U.S.C. § 112, second paragraph, is reversed.

35 U.S.C. § 112, FOURTH PARAGRAPH

The rejection of claim 8 under 35 U.S.C. § 112, fourth paragraph stands on different footing. That claim, which depends indirectly from claim 1, requires that the tether be selected from the group consisting of polyethylene oxide, carboxymethylcellulose, and starch. Reading claim 8 in light of the supporting specification, we find, according to applicants' lexicon, that carboxymethylcellulose and starch are exemplary of water-soluble, biocompatible natural polymers (specification, paragraph bridging pages 6 and 7). On these facts, we agree that claim 8 does not "specify a further limitation of the subject matter claimed" in claims 1 and 7 requiring that the tether be a water-soluble, biocompatible synthetic polymer. In light of the specification, claims 1 and 8 are internally inconsistent and we conclude that the latter does not properly depend from the former.

In the Appeal Brief and Reply Brief before the Board, applicants do not present a substantive argument addressing this ground of rejection.

The rejection of claim 8 under 35 U.S.C. § 112, fourth paragraph, is affirmed.

CLAIMS 14 THROUGH 17

We next invite attention to claims 14 through 17 on appeal, which bear close relationship to claims 1 through 4 of U.S. Patent No. 5,906,828 issued May 25, 1999, to Cima et al. For the sake of completeness, we here reproduce independent claim 13 on appeal, and dependent claims 14 through 17, as well as claims 1 through 4 of the '828 patent.

Claims On Appeal	Claims From US Patent No. 5,906,828
13. A method for growing eukaryotic cells comprising bringing into contact the cells and a composition comprising a biocompatible solid substrate, biocompatible polymeric tethers, and growth effector molecules, wherein one end of each tether is covalently linked to the substrate and each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be internalized by cells attached to the substrate, and the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules; and maintaining the contacting cells and composition under conditions and for a time sufficient to cause the cells to grow.	1. A method for growing eukaryotic cells comprising (a) bringing into contact the cells and a composition comprising a biocompatible solid substrate, biocompatible branched water soluble polymeric tethers, and growth effector molecules, wherein one end of each tether is covalently linked to the substrate, each tether is able to covalently link more than one growth effector molecule, each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be internalized by cells attached to the substrate, and the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth over the rate of target cell growth with soluble growth effector molecules and growth effector molecules adsorbed to a substrate, without internalization of the molecules; and (b) maintaining the contacting cells and composition under conditions and for a time sufficient to cause the cells to grow; wherein the step of bringing into contact comprises administering the composition to a patient in need of cell growth.
14. The method of claim 13 wherein the step of bringing into contact comprises administering the composition to a patient in need of cell growth.	
15. The method of claim 14 wherein the composition is administered by injection, infusion, or implantation.	2. The method of claim 1 wherein the composition is administered by injection, infusion, or implantation.
16. The method of claim 15 wherein the composition is administered by implantation of the composition and wherein the substrate is shaped to match a desired tissue shape.	3. The method of claim 2 wherein the composition is administered by implantation of the composition and wherein the substrate is shaped to match a desired tissue shape.
17.The method of claim 16 wherein the substrate is biodegradable.	4. The method of claim 3 wherein the substrate is biodegradable.

We have carefully reviewed the instant application and the administrative file of application 08/947,063 which issued as U.S. Patent No. 5,906,828. It is not entirely clear, however, why the PTO has maintained prior art rejections of claims 14 through 17 here, but allowed claims 1 through 4 in the '828 patent.[1] Under these circumstances, we shall vacate the examiner's decision rejecting claims 14 through 17 on prior art grounds and remand this application so that the examiner may reevaluate the patentability of those claims. Specifically, we vacate the following rejections: (1) claims 14 through 16 under 35 U.S.C. § 103(a) as unpatentable over Herweck in view of Merrill '264; (2) claim 17 under 35 U.S.C. § 103(a) as unpatentable over Herweck in view of Merrill '264 and further taken in view of Mikos; and (3) claims 14 through 17 under 35 U.S.C. § 102(b) as described by PCT '616. On remand, the examiner is not bound by the previous decision to issue U.S. Patent No. 5,906,828, i.e., the examiner is free to reject claims 14 through 17 if warranted by the prior art. Nevertheless, on remand, we recommend that the examiner take into account the issuance of the '828 patent. If, on reflection, any ground of rejection of claims 14 through 17 is entered in this application, and is also applicable to claims 1 through 4 in the '828 patent, "any letter including the rejection must have the approval of the Group Director." See Manuel of Patent Examining Procedure (MPEP) § 2307.02 (7th ed., July 1998).

On return of this application, we also recommend that the examiner evaluate whether claims 14 through 17 should be rejected for obviousness-type double

[1] The respective sets of claims are not identical. For example, claims 1 through 4 of the '828 patent require a branched tether whereas instant claims 14 through 17 do not. It does not appear, however, that the limitation of a branched tether in the patent serves to patentably distinguish over the prior art. See European Patent Application 531,733 (cited here and in Application No. 08/947,063), page 3, line 56 through page 4, line 20, disclosing a "highly branched" polyethyleneimine spacer.

patenting. Specifically, the examiner should evaluate whether entering an obviousness-type double patenting rejection of claims 14 through 17 over claims 1 through 4 of U.S. Patent No. 5,906,828 is appropriate.

CLAIMS 29, 30, AND 32

We next address the rejections of claims 29, 30, and 32 as unpatentable over a combination of references. Specifically, claims 29 and 32 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Herweck in view of Merrill '264, further taken in view of Naughton. Claims 29 and 30 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Herweck in view of Merrill '264, further taken in view of Tomomura. We agree with appellants (Appeal Brief, page 28) that the examiner has not established a prima facie case of obviousness of these claims over the cited prior art. In our judgment, the examiner's statement of these rejections (Answer, pages 10 and 11) does not set forth adequate reason, suggestion, or motivation stemming from the prior art which would have led a person having ordinary skill to combine the references in the manner proposed. Accordingly, these rejections are reversed.

THE REJECTIONS BASED ON PCT '616

In our judgment, PCT '616 constitutes the closest prior art and we now compare its disclosure with the composition sought to be patented in claim 1.

PCT '616 discloses that certain of the practical problems associated with attaching a biomolecule onto a surface can be avoided by employing a long chain chemical spacer having two reactive groups separated by a chain length of at least 25 Angstroms when extended. The length of the spacer between reactive groups is sufficient to space the biomolecule group beyond any substantial adverse interactions associated with the surface to which the spacer is attached (page 4, lines 8 through 16). According to PCT '616, "an important aspect of the invention is the discovery that adverse substrate/biomolecule interactions can be predictably reduced" (page 5, lines 22 through 24).

In one embodiment disclosed by the reference, the invention comprises a long chain spacer for tethering a biomolecule to a surface while avoiding substantial deleterious effect upon the biomolecule by the presence of the surface. The spacer comprises a chemical backbone having two reactive groups attached thereto and separated by a backbone extended chain length of not less than about 25 Angstroms, one such reactive group capable of forming a covalent bond to a surface in response to a given stimulus, and the other reactive group capable of forming a covalent bond to a biomolecule (page 5, lines 25 through 35). The bonds formed to the surface and to the biomolecule are covalent bonds (page 6, lines 31 and 32). In a further embodiment, the invention relates to a support surface, a plurality of biomolecules, and a spacer attaching and spacing the biomolecules to and from the surface, the biomolecule being spaced from the support by a distance, measured along the extended length of the spacer, of at least 25 Angstroms. In this embodiment, the spacer preferably comprises a generally hydrophilic chain having repeating units, such units preferably being

oxyalkylene groups such as ethoxy groups or isopropoxy groups (page 6, line 34 through page 7, line 8).

Respecting specific components, PCT '616 discloses biomolecules such as endothelial cell growth factor, epithelial cell growth factor, fibroblast growth factor, platelet derived growth factor, neural growth factor, and collagen (page 7, lines 14 through 27). The reference also discloses a solid support surface, preferably the surface of a "biomaterial" defined at page 8, lines 3 through 8, and having characteristics outlined at page 8, lines 9 through 23. The treated solid surface of a biomaterial is characterized as "biocompatible" if it is capable of functioning or existing in contact with biological fluid and/or tissue of a living organism with a net beneficial (not net detrimental) effect on the living organism. Long term biocompatibility is desired (page 8, lines 24 through 30). According to PCT '616, the base material of a biomaterial may be, for example, stainless steel, polyurethane, polyethylene, polytetrafluoroethylene, polypropylene, polyacrylates (including polymethacrylates), and glass (page 8, line 31 through page 9, line 16). The chemical chain backbones used as spacers in accordance with the invention may be made from a variety of chemical species, including naturally occurring and synthetic polymers, particularly homopolymers, copolymers, protein chains, and the like. The chemical chain forming the spacer backbone preferably has hydrophilic groups associated with it, such as ether groups, ketone groups, and the like. Particularly preferred are spacers having backbone chains comprising repeating units that can be made from the polymerization of various monomers and oligomers. Particularly preferred are chains having repeating ethoxy or isopropoxy groups, and of these, poly(ethylene glycol) is most preferred.

Spacer chains formed of repeating units can generally be manufactured in varying lengths; this, in turn, permits a biomolecule to be spaced by varying distances from a supporting surface. In a specific and preferred embodiment, a method disclosed by PCT '616 relates to chemically tethering a biomolecule to a supporting surface to substantially optimize the activity of the biomolecule (page 12, lines 1 through 33).

Having reviewed the PCT '616 publication in its entirety, including those passages outlined above, we find that the examiner established sound basis for believing that the compositions of claim 1 and the prior art are the same. Claim 1 recites "growth effector molecules" tethered to a biocompatible solid substrate "wherein one end of each tether is covalently linked to the substrate and each growth effector molecule is covalently linked to a distal end of a tether." PCT '616 discloses tethering "biomolecules" to a support surface using relatively long chain chemical spacers or tethers and covalent bonds "while avoiding substantial deleterious effect upon the biomolecule by the presence of the surface" (page 5, lines 27 and 28). In the judgment of this merits panel, these tethered compositions reasonably appear to be the same and the examiner has established a prima facie case of anticipation.

> Applicants point to this functional limitation or "so that" clause recited in claim 1:
>
> so that the growth effector molecule cannot be internalized by cells attached to the substrate, and the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules.

Applicants argue that claim 1 distinguishes over PCT '616 in view of that limitation. We disagree. We do not have the laboratory facilities to confirm, by experiment, that the above-quoted functional limitation is an inherent characteristic of the prior art.

Nevertheless, on this record, the burden of persuasion rests on applicants to prove that the compositions of PCT '616 do not possess the characteristic relied on. This applicants have not done. We have reviewed the experimental work reported in applicants' specification, including figures 1 and 2. Manifestly, that specification evidence is not designed to prove, and does not prove, that the compositions of PCT '616 do not inherently possess the characteristics recited in applicants' "so that" clause.

As stated in In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977),

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.... Whether the rejection is based on 'inherency' under 35 U.S.C. § 102, on 'prima facie obviousness' under 35 U.S.C. § 103, jointly, or alternatively, the burden of proof is the same, and its fairness is evidenced by PTO's inability to manufacture products or to obtain and compare prior art products [citations and footnote omitted].

Likewise, when the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not. In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Again, as stated in In re Swinehart, 439 F.2d 210, 212-13, 169 USPQ 226, 229 (CCPA 1971),

> it is elementary that the mere recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not cause a claim drawn to those things to distinguish over the prior art. Additionally, where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on.

Following those principles of law, we find that the examiner established a prima facie case of anticipation of claim 1 in view of PCT '616; and that applicants have not rebutted the prima facie case. Therefore, we affirm the rejection of claim 1 under 35 U.S.C. § 102(b) as described by PCT '616.

Respecting the ground of rejection under 35 U.S.C. § 102(b) based on PCT '616, applicants do not present separate, substantive arguments for claims 2 through 10, 12, 13, 18 through 26, 28, or 31. Accordingly, those claims fall together with claim 1. See 37 CFR § 1.192(c)(7) and (c)(8) (1997). The rejection of claims 2 through 10, 12, 13, 18 through 26, 28, and 31 under 35 U.S.C. § 102(b) as described by PCT '616 is affirmed.

Claims 11 and 27 stand rejected under 35 U.S.C. § 103(a) as unpatentable over PCT '616 (Answer, page 14). These claims place a limitation on the backbone length of applicants' tether. The examiner argues that, although the invention recited in these claims is not identically described in PCT '616, nevertheless, the claimed subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. In their briefings before us, applicants do not address these claims separately or present a substantive argument controverting the examiner's position. As best we can understand, applicants argue that the functional limitation or "so that" clause of claim 1 not only distinguishes that claim over the cited prior art, but claims 11 and 27 as well. We disagree. In the absense of a separate argument addressing the merits of the examiner's position respecting claims 11 through 27, we summarily affirm the rejection of those claims under 35 U.S.C. § 103(a) as unpatentable over PCT '616.

HE § 102 REJECTION BASED ON EP '733

We now consider the examiner's rejection of claim 1 under 35 U.S.C. § 102(b) as described by EP '733.

EP '733 discloses a carrier for animal cell culture which can maintain and enhance the function of cells, and promote cell growth after cells adhered to the carrier. The carrier comprises a base material having a three-dimensional network-type porous structure, wherein a cell adhesive factor and a cell growth factor are immobilized on a surface of a carrier (page 2, lines 40 through 48). The cell adhesive factor is a factor for enabling the cell adhesivity inherent in the cells, i.e., a property such that cells adhere to each other or to the surface of a solid other than cells, to be exhibited. Examples of this factor include, inter alia, proteins such as fibronectin, laminin, and collagen (page 2, lines 52 through 57). The cell growth factor is a factor which acts on cells to regulate the growth and, in some cases, differentiation of cells. Specific examples of cell growth factors include, inter alia, epidermal growth factor (EGF), platelet derived growth factor (PDGF), fibroblast growth factor family (FGF-family), insulin-like growth factor (IGF), and endothelial growth factor (ECGF) (page 3, lines 20 through 25).

According to a preferred embodiment described by EP '733, the cell adhesive factor and the cell growth factor are linked to the surface of the carrier through a so called "spacer" which enables the base material and the factors to be held together while keeping them apart at a given distance and maintaining a three-dimensional degree of freedom. It is advantageous for factors to be held on the surface of the carrier through a spacer because, in this way, the factors can bind to a receptor even

when that receptor is not in the vicinity of the surface of cells in contact with the carrier. The distance between these factors and the carrier, that is, the length of the spacer, can be determined by a person having ordinary skill in the art by taking into consideration the kinds of factors and cells and the like. The expression "holding the factors while maintaining a three-dimensional degree of freedom" refers to a degree of freedom such that the factors can freely change their position within a given space without being fixed to a particular position (page 3, lines 41 through 55).

According to a further preferred embodiment described by EP '733, a polymer is suitable as the spacer. Preferred examples of polymers useful for this purpose include, inter alia, polyethyleneimine, polyamino acid, and polymethylene. The linkage of the spacer with the cell adhesive factor and the cell growth factor and the carrier can be properly practiced by using a functional group present in the factors, the spacer, and the carrier (page 3, line 56 through page 4, line 25).

The carrier for animal cell culture has a "three-dimensional network structure," i.e., a structure having continuous pores of such size that animal cells can be cultivated therein. Preferably, the base material comprises a foam having a porosity of 80% or more, preferably 95% or more, still preferably 97% or more and a mean pore diameter of 0.03 to 2.0 mm, preferably 0.1 to 1.5 mm. When the porosity and mean pore diameter of the base material are in the above-described respective ranges, cells grow, and no necrosis occurs even in cells present in the deep part of the carrier. The base material preferably comprises a foam of a naturally occurring polymer, e.g., cellulose (page 4, lines 29 through 42). As described in EP '733, the carrier for animal cell culture has a surface which allows an excellent adhesion and promotes growth of

unlimited types of cells, and can also be applied to serum-free cultivation. Specific examples of the animal cells which may be adhered and grown in these carriers include, inter alia, fibroblasts and hepatocytes (page 5, lines 16 through 28). In example 1, step (3), EP '733 describes how a polyethyleneimine "spacer" was linked to a base material comprising cellulose foam and, subsequently, how the cell adhesive factor and the cell growth factor were linked to polyethyleneimine linked to the base material (page 6, lines 1 through 22).

Having reviewed the EP '733 reference in its entirety, including those passages outlined above, we find that the examiner established sound basis for believing that the compositions of claim 1 and the prior art are the same. Claim 1 recites "growth effector molecules" tethered to a biocompatible solid substrate "wherein one end of each tether is covalently linked to the substrate and each growth effector molecule is covalently linked to a distal end of a tether." EP '733, in comparison, discloses a "cell adhesive factor" and "cell growth factor" linked to the surface of a carrier for animal cell culture by a "spacer" enabling the base material and the factors to be held together while keeping them apart at a given distance and maintaining a three-dimensional degree of freedom (page 3, lines 43 and 44). It appears to us that the polymers, suitable for use as spacers in EP '733, meet the terms of "biocompatible synthetic polymeric tethers" recited in claim 1. Further, applicants do not deny that the spacer in EP '733 is covalently linked to the base material, or that the cell adhesive factor and cell growth factor are covalently linked to the spacer linked to the base material. In the judgment of this merits panel, these respective compositions reasonably appear to be the same and the examiner has established a prima facie case of anticipation. In other words, on this

record, it appears that EP '733 discloses each and every element recited in claim 1 on appeal; and that the elements in the prior art are arranged in the same way as those set forth in claim 1 on appeal.

Again, applicants rely on this functional limitation or "so that" clause recited in claim 1:

> so that the growth effector molecule cannot be internalized by cells attached to the substrate, and the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules.

Applicants argue that claim 1 distinguishes over EP '733 in view of that limitation. We disagree. We do not have the laboratory facilities to confirm, by experiment, that the above-quoted functional limitation is an inherent characteristic of the prior art. Nevertheless, on this record, the burden of persuasion rests on applicants to prove that the compositions of EP '733 do not possess the characteristic relied on. This applicants have not done. We have reviewed the experimental work reported in applicants' specification, including Figures 1 and 2. Manifestly, that specification evidence is not designed to prove, and does not prove, that the compositions of EP '733 do not inherently possess the characteristics recited in applicants' "so that" clause.

Referring to Figure 2 in the specification and the accompanying description at page 24, lines 4 through 22, applicants argue that their tethered growth effector molecules enhance cell growth compared to adsorbed growth effector molecules (Appeal Brief, paragraph bridging pages 17 and 18; Reply Brief, paragraph bridging pages 5 and 6). Applicants argue that the composition of EP '733 is "similar" to the adsorbed growth effector molecules in that comparison, i.e., that Figure 2 shows

enhanced cell growth for applicants' tethered growth effector molecules compared to adsorbed growth effector molecules "similar" to the composition of EP '733 (Appeal Brief, page 17; Reply Brief, page 5). That is not enough. On this record, applicants have not established that the closest prior art compositions described by EP '733 do not inherently possess the characteristics recited in applicants' "so that" clause.

As stated in In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977),

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.... Whether the rejection is based on "inherency" under 35 U.S.C. § 102, on "prima facie obviousness" under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [citations and footnote omitted].

Likewise, when the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicants have the burden of showing that they are not. In re Spada, 911 F.2d 705,708, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Again, as stated in In re Swinehart, 439 F.2d 210,212-13, 169 USPQ 226, 229 (CCPA 1971)

> It is elementary that the mere recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not cause a claim drawn to those things to distinguish over the prior art. Additionally, where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on.

Following those principles of law, we find that the examiner established a prima facie case of anticipation of claim 1 in view of EP '733; and that applicants have not rebutted the prima facie case. Therefore, we affirm the rejection of claim 1 under 35 U.S.C. § 102(b) as described by EP '733.

Respecting the ground of rejection under 35 U.S.C. § 102(b) based on EP '733, applicants do not present separate, substantive arguments for claims 2 through 7, 9, 10, 13, 18 through 21, 23, 25, 26, 29, 30, and 31. Accordingly, those claims fall together with claim 1. See 37 CFR § 1.192(c) (7) and (c) (8) (1997). The rejection of claims 1 through 7, 9, 10, 13, 18 through 21, 23, 25, 26, 29, 30, and 31 under 35 U.S.C. § 102(b) as described by EP '733 is affirmed.

CONCLUSION

In conclusion, for the reasons set forth in the body of this opinion, we reverse the rejection of claims 1 through 32 under 35 U.S.C. § 112, second paragraph, but affirm the rejection of claim 8 under 35 U.S.C. § 112, fourth paragraph. We vacate the examiner's decision rejecting claims 14 through 17 and remand this application so that the examiner may reevaluate the patentability of those claims on prior art grounds and on the ground of obviousness-type double patenting. We reverse the rejections of claims 29, 30, and 32 as unpatentable over a combination of references. We affirm the rejection of claims 1 through 10, 12, 13, 18 through 26, 28, and 31 under 35 U.S.C. § 102(b) as described by PCT '616, and we also affirm the rejection of claims 11 and 27 under 35 U.S.C. § 103(a) as unpatentable over PCT '616. Finally, we affirm the

rejection of claims 1 through 7, 9, 10, 13, 18 through 21, 23, 25, 26, 29, 30, and 31 under 35 U.S.C. § 102(b) as described by EP '733.

In view of our disposition of this appeal, we find it unnecessary to discuss the rejection of (1) claims 1 through 9, 13, 18 through 25, and 31 under 35 U.S.C. § 102(b) as described by Clapper; (2) claims 10 through 12 and 26 through 28 under 35 U.S.C. § 103(a) as unpatentable over Clapper; (3) claims 1 through 9, 13, 18 through 25, and 31 under 35 U.S.C. § 103(a) as unpatentable over Herweck in view of Merrill '264; (4) claims 10 through 12 and 26 through 28 under 35 U.S.C. § 103(a) as unpatentable over Herweck in view of Merrill '264, further taken in view of Merrill (J. of Biomater. Sci. Polymer); and (5) claims 10 through 12 and 26 through 28 under 35 U.S.C. § 103(a) as unpatentable over EP '733.

The examiner's decision rejecting claims 1 through 13 and 18 through 31 is affirmed. The decision rejecting claim 32 is reversed. The decision rejecting claims 14 through 17 on prior art grounds is vacated and the application is remanded to the examiner for further consideration of those claims.

AFFIRMED-IN-PART,

REVERSED-IN-PART; and

VACATED AND REMANDED-IN-PART

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